REMARKS

Rejections Under 35 USC §102

Claims 1, 2, 4, 6 and 10 are rejected under 35 U.S.C. §102(e) as being anticipated by Jain et al. (U.S. Pat. No. 6,010,712). Applicant respectfully traverses this rejection.

Claim 1 is drawn to a method of using basic fibroblast growth factor (b-FGF) to treat endotoxic shock in an animal by inhibiting the generation of ceramide from sphingomyelin. Claim 4 is drawn to a method of using b-FGF to inhibit endothelial apoptosis resulting from endotoxic shock in an animal. Claim 10 recites a method of treating an individual at risk for sepsis by administering b-FGF, where b-FGF prevents endothelial apoptosis resulting from sepsis. An example of such prevention is shown by the specification on page 27, lines 1-21, and in Figures 6A-6B. When administered concomitantly with LPS, b-FGF was able to abrogate LPS-induced apoptosis in the intestine and lung of treated mice; such abrogation was not total, but would necessarily involve substantial prevention of apoptosis in order to allow endothelial cell survival. Administration of b-FGF also enhanced the survival of LPS-treated mice, showing that b-FGF was effective in preventing the development of sepsis (Figure 6B).

Jain et al. teach a method of using b-FGF to decrease cell surface expression of ICAM-1 or VCAM-1 on endothelial cells, thereby reducing adhesion of cytotoxic white cells to vascular endothelium (see abstract). The Examiner contends that **Jain** et al. disclose a method of treating sepsis by administering b-FGF to an animal suffering from said condition. Applicant respectfully disagrees.

Applicant submits that **Jain** et al. do not provide an enabling disclosure for a method of using b-FGF to treat sepsis. **Jain** et al. only present *in vitro* data that show the effects of b-FGF on white cell adhesion to vascular endothelium. Although **Jain** et al. demonstrate inhibition of cytotoxic white cells adhesion to vascular endothelium by b-FGF, **Jain** et al. do not show inhibition of cytotoxic white cells adhesion to vascular endothelium would provide a treatment for sepsis. Endotoxic shock or sepsis is a complex biological event that involves multiple cell types and processes. Cell adhesion to endothelium is only one of various events occurring during sepsis. **Jain** et al. do not teach cytotoxic white cells adhesion to vascular endothelium is such a critical event in sepsis that inhibition of cell adhesion to vascular endothelium would affect the process of sepsis or provide treatment for sepsis.

In view of the complex cellular processes of sepsis involving more than white cell adhesion to endothelium, one of ordinary skill in the art would have no basis to conclude that inhibiting cell adhesion by b-FGF would provide treatment for sepsis in the absent of data showing the efficacy of b-FGF *in vivo*. The data of *in vitro* cell adhesion inhibition shown in **Jain** et al. do not show b-FGF would have beneficial effects *in vivo*. One of ordinary skill in the art must determine the effects of b-FGF treatment by *in vivo* experiments such as those shown in the present specification. In conclusion, **Jain** et al.'s claim of treating sepsis with b-FGF does not commensurate with the scope of enablement provided in the disclosure. One of ordinary skill in the art could practice a method of treating sepsis by b-FGF only after the disclosure of the present invention.

In view of the above remarks, Applicant submits that **Jain** et al. do not teach each and every aspect of the present invention because of lack of enablement. Accordingly, Applicant respectfully requests that the rejection of claims 1, 2, 4, 6 and 10 under 35 U.S.C. §102(e) be withdrawn.

Rejections Under 35 USC §103(a)

Claims 1, 3, 4 and 7 are rejected under 35 U.S.C. §103(a) as being unpatentable over **Jain** et al. Applicant respectfully traverses this rejection.

The present invention and the teaching of **Jain** et al. have been discussed above. As discussed above, the claim of sepsis treatment in **Jain** et al. is a mere proposal that invites further experimentation by one of ordinary skill in the art. Furthermore, **Jain** et al. do not provide reasonable expectation of success of treating sepsis with b-FGF. Cell adhesion to endothelium is only one of various events occurring during sepsis. **Jain** et al. do not teach cytotoxic white cells adhesion to vascular endothelium is such a critical event in sepsis that inhibition of cell adhesion to vascular endothelium would affect the process of sepsis or provide treatment for sepsis. The data of *in vitro* cell adhesion inhibition shown in **Jain** et al. do not show b-FGF would have beneficial effects *in vivo*. In view of the data shown in **Jain** et al., b-FGF may or may not have beneficial effects *in vivo*. One of ordinary skill in the art must determine the effects of b-FGF treatment by *in vivo* experiments such as those shown in the present specification.

In view of the above remarks, **Jain** et al. do not provide a person having ordinary skill in this art with the requisite expectation of successfully producing Applicant's claimed methods. The invention as a whole is not *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicant respectfully requests that the rejection of claims 1, 3, 4 and 7 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Final Office Action mailed June 24, 2003. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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